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The National Center for Post-Traumatic Stress Disorder

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VA COOPERATIVE STUDY # 334: I. SUMMARY OF FINDINGS ON THE PSYCHOPHYSIOLOGICAL ASSESSMENT OF PTSD

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Studies of the psychophysiology of PTSD can be traced to the observations of Kardiner (1941), who viewed the psychological sequelae of combat as a "physioneurosis." He characterized patients with this condition as having obvious elevations in muscle tension, tachycardia, startle response, and a hyperresponsivity to external stimulation. These observations led to empirical studies by Wenger (1948) and then Dobbs and Wilson (1960), which found that physiological and psychophysiological measures distinguished veterans with combat stress disorders from a variety of comparison groups of veterans. The clinical observations of Kardiner and the empirical studies of a variety of scientists, including Grinker and Spiegel (1945), established the foundation for contemporary studies of the psychophysiology of PTSD among Vietnam veterans.

The purpose of this report is to update the field on the status of a multi-site clinical trial that examined the ability of psychophysiological responses to predict PTSD diagnosis in a large sample of male Vietnam veterans. Data were collected from 1990 to 1992 at 15 clinical research laboratories in VA Medical Centers in the United States. The scientific premise of the study came from a series of publications, reflecting work of three independent research groups, that demonstrate how combat veterans with PTSD can be distinguished from combat veterans without PTSD on the basis of psychophysiological information. A large-scale study was needed to determine the generalizability of the accumulated findings to a broader sample of help-seeking veterans. Such an effort would strengthen the scientific foundation for this type of assessment and help clarify its diagnostic implications for a larger segment of the VA population.

Three studies conducted in the 1980s served as the contemporary foundation for the multi-site project. The first of these, by Blanchard et al. (1982), found that psychophysiological responses to standardized sounds of combat discriminated Vietnam veterans with PTSD from an age and gender matched comparison group. At about the same time, Malloy et al. (1983) employed standardized audiovisual cues of neutral and combat situations while measuring heart rate, skin resistance, and subjective distress. Male Vietnam veterans with PTSD were found to be more physiologically responsive to the combat cues compared to veterans with psychiatric impairment (but without PTSD) and veterans with no psychiatric impairment. The third influential study was conducted by Pitman et al. (1987). These investigators adapted Peter Lang's (1985, 1995) imagery-based methods for studying the psychophysiology of emotion and set about comparing Vietnam veterans with and without PTSD on heart rate, skin conductance, and facial electromyographic responses. The study used a set of 30-second imagery scripts that were constructed in a systematic fashion so that each contained stimulus, response, and meaning elements. Scripts depicted individually-tailored traumatic and non-traumatic (e.g., neutral) experiences that were compared to one another in terms of the physiological and subjective reactions they produced. Results based on this procedure demonstrated again that veterans with PTSD react to individually-relevant combat cues with greater arousal and distress than do veterans without PTSD.

These and other studies from a number of laboratories provided impressive preliminary evidence that individuals who qualify for a PTSD diagnosis can be discriminated from those who do not meet PTSD criteria when the groups are compared on their psychophysiological response to challenge tasks that involve presentation of trauma-relevant cues (see Orr & Kaloupek, 1997; Prins et al., 1995). Despite the impressive consistency of findings, there are methodological limitations that raise questions about the individual estimates of diagnostic accuracy obtained by any particular study in the set. These limitations include: (a) problems of inflated base rates due to the fact that PTSD patients typically comprised 1/3 to 1/2 of the study sample, a higher rate than is likely to occur in the population at large; (b) several of the comparison groups consisted of veterans who were not seeking help for their problems (e.g., VA health services) while participants in the PTSD group were; (c) only two studies (Blanchard et al., 1991; Orr et. al., 1993) attempted to cross-validate findings within the context of a single study; and (d) most of the studies did not employ contemporary multivariate data analytic strategies to investigate classification accuracy.

Many of the studies conducted during the 1980s

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found classification rates of 75-95% when psychophysiological variables were used for post hoc classification relative to interview-based PTSD diagnosis. This places psychophysiological responses to a trauma-relevant challenge task among the most reliable and robust physiological indicators of any psychological disorder or condition. This high level of promise, coupled with the previously noted methodological limitations, provided justification for a more definitive study that would collect data from a large sample of subjects in order to test the utility of psychophysiological reactivity as an index of PTSD. A proposal was submitted to the VA Cooperative Studies Program by principal investigators Terence Keane and Lawrence Kolb because it was recognized that a suitably large sample of individuals with PTSD would be difficult to accumulate at one site within a reasonable time period. The Cooperative Studies research operation was well suited to the task because it specializes in multi-site investigations that capitalize on the exceptional research talent and large patient populations available across the VA system.

In time, the proposal successfully negotiated the rigors of the Cooperative Studies Program, and Cooperative Study #334 was initiated. The goals of the project included conducting a comprehensive utility analysis of psychophysiological variables in order to generate indices of sensitivity, specificity, predictive power of a positive test, and predictive power of a negative test. These components of a psychometric analysis are typically used in the development of any new psychological or medical test. As a set, they provide a comprehensive understanding of the accuracy associated with a particular measurement tool.

Method. CS #334 was directed from the Chair's office at the Boston VAMC, with operational support from the Cooperative Studies Program Coordinating Center in Menlo Park, CA. Fifteen sites were selected in a competition involving forty-three medical centers that submitted full applications expressing interest in serving as a participating site. Training for the study included a centralized workshop for study clinicians devoted to administration of diagnostic interviews, and a similar workshop for study technicians concerning the laboratory procedures and data management. The workshops were supplemented by on-site consultation with an expert on psychophysiological measurement, as well as regularly scheduled telephone conference calls involving all site investigators and project directors. Ongoing telephone supervision and consultation with experts was routinely available for any problems that arose after the study was initiated. In addition, an annual meeting of project staff from all fifteen sites was organized to present updated information and to resolve collective difficulties that sites identified.

Participants. Primary recruitment sources for the project included VA Medical Center inpatient and outpatient programs in psychiatry, substance abuse, and PTSD. All participants were male, had served in the Vietnam theater of operations between August 1964 and May 1975, and were receiving some form of service from DVA. Individuals were excluded from participation if they experienced cardiovascular disease including stroke, myocardial infarction, angina, or uncontrolled hypertension. Individuals also were excluded if they were diagnosed with an endocrine disorder, seizure disorder, or organic brain syndrome. Participants were required to be free of psychotropic medications or beta-andrenergic blocking medication, though individuals who were taking such medications at the time of screening remained eligible if they and their physician agreed to medication withdrawal through the period of the study. Acute alcohol use and illicit drug use during the course of the study were restricted, and urine samples were obtained to ensure compliance with this regulation. A total of 2,115 individuals were screened as potential participants, and 654 were excluded on the basis of factors listed above. Of the 1,461 veterans eligible for participation, 220 terminated prior to the psychophysiological testing, including 133 who did so before completing the diagnostic interview for PTSD.

Psychological Assessment. Because there is no absolute criterion, no "gold" standard, for the measurement and diagnosis of PTSD, a decision had to be made about how best to establish the diagnosis for the purposes of the study. The instrument selected for this purpose was the PTSD module of the Structured Clinical Interview for the DSM-III-R (SCID; Spitzer et al., 1989), arguably the most widely used PTSD interview format available at the time. Positive features of the module included its administration by clinically trained individuals, the available pool of VA clinicians who had experience using the interview with PTSD patients, and the fact that the module was part of a comprehensive instrument that could be used for other diagnostic determinations in the study.

During actual data collection, the War Stress Interview (Rosenheck & Fontana, 1989) was administered first to obtain sociodemographic, psychosocial history, and mental health information. Participants next completed the SCID, including modules for major depression, bipolar disorder, schizophrenia, alcohol abuse and drug abuse, panic disorder, social phobia, obsessive-compulsive disorder, dissociative disorder, and PTSD (combat-related and non-combat related). Antisocial and borderline personality disorders were assessed using modules of the SCID-II. All interviews were audiotaped, and a selected subset was employed in a study of interater reliability.

The SCID interview was completed by 1,328 participants who were assigned to the following groups: Current PTSD (n = 778), Lifetime PTSD (n = 181) and Never PTSD (n = 369). After the WSI and SCID, participants completed the MMPI-2, which contains the Keane PTSD scale (Keane et al., 1984), as well as the Combat Exposure Scale (Keane et al., 1989), the Mississippi Scale for Combat Related PTSD (Keane et al., 1988), and the Laufer Parsons Inventory (Laufer et al., 1981) to assess combat-related guilt.

Psychophysiological Assessment. The study applied both the standardized audiovisual format developed by Malloy et al. (1983) and the idiographic imagery format used by Pitman et al. (1987). Psychophysiologic measures included heart rate, skin conductance, forehead electromyogram,

and systolic and diastolic blood pressure.

The procedures for all sites were identical and standardized from minute to minute throughout the course of the laboratory tasks. All participants were introduced to the psychophysiological laboratory on a separate day after completing both the diagnostic interviewing and psychological assessment. They were first oriented to the laboratory before sensors were attached for physiological recording. At the start of the procedure, each participant was asked to relax quietly for a period of 10 minutes. Next, they engaged in mental arithmetic, a generic stressor task, for 2 minutes before sitting quietly for a 5-minute rest period. The next phase of the laboratory procedure included presentation of a set of 6 standardized neutral audiovisual presentations that lasted 1 minute each. These consisted of 6 still pictures and an accompanying sound track presented for 1 minute each. Physiological measures were recorded during each presentation and subjective ratings of distress (SUDS) were obtained during a 30 second period between presentations. The neutral presentations were followed by a 5-minute rest period, which was followed by presentation of 6 combat audiovisual scenes according to the same procedure used for the neutral scenes. The combat scenes were followed by a 5-minute recovery period.

Following another 5-minute rest period, participants were presented a set of 4 tape-recorded imagery scripts, each of which consisted of 4 sequential 30-second periods: the baseline, reading of the script, imagining the script, and recovery. Two of the imagery scripts (the first and third in the sequence) had neutral content that was standardized across subjects. The other two scripts depicted the two most upsetting or stressful combat experiences identified by the participant during a special interview conducted by the study clinician in conjunction with the diagnostic interviewing. A 5-minute recovery period concluded the psychophysiological assessment procedure.

Most participants were debriefed about the study—not just the laboratory session—after the recording sensors were removed. However, a subset of approximately 25% of the participants was randomly selected for a second laboratory testing that was scheduled on a separate day to examine the stability or test-retest reliability of the physiological assessment procedures. Debriefing for these participants followed the second challenge test session.

Primary data analysis for the study used logistic regression to predict membership in Current PTSD or Never PTSD groups. The total study group with completed psychophysiological testing ($n = 1,241$) was divided randomly into two samples so that the resulting prediction equation could be cross-validated. The calibration sample that generated the equation was comprised of approximately two-thirds ($n = 740$) of the participants. The validation sample to which the equation was re-applied was comprised of the remaining one-third ($n = 371$).

Findings. Results of this multi-site investigation provide definitive support for relatively heightened physiological responsivity to combat cues for male veterans with a PTSD diagnosis. The response differences are, predictably, greatest between the Current PTSD and Never PTSD groups. The differences are found in conjunction with both the standardized audiovisual format and the idiographic imagery format of challenge testing.

In addition, higher absolute levels of physiological measures were found at baseline for the Current PTSD group. These differences specifically involve heart rate and skin conductance measures and suggest that individuals with current PTSD are more aroused at rest than those in the other two groups. Similar differences have been reported by several of the previous small-scale studies, and we (Prins et al., 1995) have interpreted them as an indication of anticipatory fear triggered in veterans with PTSD who find novel environments such as a psychophysiology laboratory to be threatening. A recent study by Orr and his colleagues (1998) adds to the evidence that veterans with PTSD do not show differences in resting physiological measures when they are at home, in a presumably nonthreatening environment. Such evidence argues against the notion of fixed physiological elevations among individuals with PTSD and is consistent with situational influences on baseline arousal such as anticipatory anxiety.

It was evident that the absolute level of responding to trauma-related cues was lower in this study than in many of the prior studies. This comparative reduction may well be attributable to the application of stringent inclusion and exclusion criteria that limited participation to relatively healthy subjects who were willing and able to come off their psychotropic medications.

Some findings relevant to the magnitude of responding by the study participants come from follow-up analysis of responders and non-responders within the current PTSD group. This analysis demonstrates that the most responsive individuals show heart rate increases of 6-7 beats per minute, consistent with values obtained in the earliest studies. These Responders also displayed selectively greater symptoms of PTSD, and more symptoms of war-related guilt and depression on self-report scales. It is quite possible that application of the inclusion/exclusion criteria caused the study to enroll a broader range of PTSD severity than had the preliminary studies in the field, particularly at the lower end of the severity spectrum.

Using physiological variables alone, the optimal percentage for correct classification was 69% in the calibration sample and 64% in the validation sample, yielding a combined rate of approximately 67%. These results are lower than those previously reported, but some of this reduction was expected because the sampling strategy differed from past efforts by emphasizing the absence of medications or drugs as potential influences on the physiological variables. Nonetheless, the results are quite respectable for a *biological test* of a *psychological* condition, surpassing classification rates observed in other such arenas (e.g., the Dexamethasone Suppression Test for Depression; Insel & Goodwin, 1983).

In terms of the participants who met criteria for a lifetime PTSD diagnosis, we initially predicted that they would

show physiological reactivity that ranged between that shown by the Current PTSD and Never PTSD groups. This was generally the case. For the test-retest reliability component of the project, we learned that over a period of approximately 10 days there was a significant reduction in responsiveness overall, but the level of consistency (e.g., relative rank for an individual) across the two assessments was quite high.

In conclusion, CS #334 provides strong empirical support for the presence of objectively measured psychophysiological reactivity to trauma cues as a distinguishing feature of PTSD. The findings suggest that individuals with the strongest physiological responses are the most impaired on clinical self-rating scales, and they endorsed more symptoms of war-related guilt and depression. Finally, the findings from the array of psychological tests, questionnaires, and interviews employed in the study indicate that Vietnam veterans with current PTSD continue to suffer from a broad range of psychological symptoms, multiple comorbid conditions, marital and family dysfunction, vocational impairment, financial instability, and other psychosocial difficulties. The extent to which these findings regarding psychophysiological and cardiac reactivity can predict service utilization, the development of additional health problems, and continued psychological distress remains an important empirical question that warrants additional study.

REFERENCES

BLANCHARD, E.B., KOLB, L.C., PALLMEYER, T.P., & GERARDI, R.J. (1982). **A psychophysiological study of posttraumatic stress disorder in Vietnam veterans.** *Psychiatric Quarterly, 54,* 220-229.

BLANCHARD, E.B., KOLB, L.C., & PRINS, A. (1991). **Psychophysiological responses in the diagnosis of posttraumatic stress disorder in Vietnam veterans.** *Journal of Nervous and Mental Disease, 179,* 99-103.

DOBBS, D. & WILSON, W.P. (1960). **Observations on persistence of war neurosis.** *Diseases of the Nervous System, 21,* 686-691.

GRINKER, R.R. & SPIEGEL, J.P. (1945). *Men under stress*. Philadelphia: Blakiston.

INSEL, T.R. & GOODWIN, F.K. (1983). **The dexamethasone suppression test: Promises and problems of diagnostic laboratory tests in psychiatry.** *Hospital and Community Psychiatry, 34,* 1131-1138.

KARDINER, A. (1941). *The traumatic neuroses of war*. New York: Hoeber.

KEANE, T.M., CADDELL, J.M., & TAYLOR, K.L. (1988). **Mississippi Scale for Combat-Related Posttraumatic Stress Disorder:Three studies in reliability and validity.** *Journal of Consulting and Clinical Psychology, 56,* 85-90.

KEANE, T.M., FAIRBANK, J.A., CADDELL, J. M., ZIMERING, R. T., TAYLOR, K. L., & MORA, C. A. (1989). **Clinical evaluation of a measure to assess combat exposure.** *Psychological Assessment, 1,* 53-55.

KEANE, T.M., MALLOY, P.F., & FAIRBANK, J.A. (1984). **Empirical development of an MMPI subscale for the assessment of combat-related posttraumatic stress disorder.** *Journal of Consulting and Clinical Psychology, 52,* 888-891.

LANG, P.J. (1985). **The cognitive psychophysiology of emotion: Fear and anxiety.** In A. H. Tuma & J.D. Maser (Eds.), *Anxiety and the anxiety disorders* (pp. 131-170). Hillsdale, NJ: Erlbaum.

LANG, P.J. (1995). **The emotion probe: Studies of motivation and attention.** *American Psychologist, 50,* 372-385.

LAUFER, R.S., YAGER, T., FREY-WOUTERS, E., & DONNELLAN, J. (1981). *Legacies of Vietnam, vol. III: Post-war trauma: Social and psychological problems of Vietnam veterans in the aftermath of the Vietnam War*. Washington, D.C.: U.S. Government Printing Office.

MALLOY, P.F., FAIRBANK, J.A., & KEANE, T.M. (1983). **Validation of a multimethod assessment of posttraumatic stress disorders in Vietnam veterans.** *Journal of Consulting and Clinical Psychology, 51,* 488-494.

ORR, S.P. & KALOUPEK, D.G. (1997). **Psychophysiological assessment of posttraumatic stress disorder.** In J.P. WILSON, & T.M. KEANE (Eds.), *Assessing psychological trauma and PTSD: a handbook for practitioners* (pp. 69-97). New York: Guilford.

ORR, S.P., MEYERHOFF, J.L., EDWARDS, J.V., & PITMAN, R.K. (1998). **Heart rate and blood pressure resting levels and responses to generic stressors in Vietnam veterans with posttraumatic stress disorder.** *Journal of Traumatic Stress 11,* 155-164.

ORR, S.P., PITMAN, R.K., LASKO, N.B., & HERZ, L.R. (1993). **Psychophysiological assessment of posttraumatic stress disorder imagery in World War II and Korean combat veterans.** *Journal of Abnormal Psychology, 102,* 152-159.

PITMAN, R.K., ORR, S.P., FORGUE, D.F., DE JONG, J.B., & CLAIBORN, J. M. (1987). **Psychophysiologic assessment of posttraumatic stress disorder imagery in Vietnam combat veterans.** *Archives of General Psychiatry, 44,* 970-975.

PRINS, A., KALOUPEK, D.G., & KEANE, T.M. (1995). **Psychophysiological evidence for autonomic arousal and startle in traumatized adult populations.** In M. J. Friedman, D. S. Charney & A. Y. Deutch (Eds.), *Neurobiological and clinical consequences of stress: from normal adaptation to post-traumatic stress disorder* (pp. 291-314). Philadelphia: Lippincott-Raven.

ROSENHECK, R. & FONTANA, A. (1989). *War Stress Interview (WSI)*. West Haven, CT: Department of Veterans Affairs, Northeast Program Evaluation Center.

SPITZER, R.L., WILLIAMS, J. B.W., GIBBON, M., & FIRST, M. D. (1989). *Structured Clinical Interview for DSM-III-R—patient version (SCID-P)*. New York: New York State Psychiatric Institute, Biometrics Research Division.

WENGER, M.A. (1948). **Studies of autonomic balance in army air forces personnel.** *Comparative Psychology Monographs, 19.*

VA COOPERATIVE STUDY #334: II. OVERVIEW OF THE PLANNING PROCESS

Many investigators feel that the Cooperative Studies Program of the Office of Research and Development in the Department of Veterans Affairs is the crown jewel in an extraordinarily productive research program. The Cooperative Studies Program capitalizes on the exceptional pool of professional talent associated with VA research and clinical programs, and the large number and wide geographic distribution of VA facilities as a vehicle for conducting multi-site clinical trials. The tremendous success and broad impact of the program on health care is evident in a roster of studies that includes monumental investigations such as those examining the effects of aspirin on heart disease and testing treatments for hypertension.

Not surprisingly, the first step in developing a Cooperative Study proposal involves gaining familiarity with the practices and procedures for accessing the program. While this step can appear daunting for investigators accustomed to individual VA Merit Review or NIH grant applications, the logic of the program requirements becomes apparent when one considers the need to manage the complexity of a large research enterprise and the cost of a multi-site initiative. Mechanisms are in place to insure that the proposal is feasible in terms of coordination and that it is likely to produce findings that justify the costs involved. With these considerations in mind, Cooperative Study #334 was based on an idea supported by a substantial body of evidence drawn from a number of projects conducted by individual investigators over nearly a decade.

The first formal stage in a Cooperative Study proposal is submission of a Planning Request. This document is similar to the brief Letter of Intent that often precedes proposal submission for individual grant programs. The principal proponent for the study submits a ten-page request that contains the objectives of proposed research, the importance of the topic to the VA, justification and need for multi-site study, a review of the literature, and a brief description of the proposed study design. The description of the study design need not contain all details of the proposed study. Indeed, this study description aims to demonstrate to reviewers the logical integration of the questions posed, the design considered, the data to be collected, and the outcomes to be measured, as well as the importance of the questions in clinical and, especially, scientific context.

The Planning Request is submitted to the Chief Research and Development Officer through the local VA Research and Development Office. Approval of the plan requires favorable evaluation from the CSP review panel. If approved, the proposal is assigned to a specific coordinating center, a study biostatistician is allocated to the project, and detailed planning begins. CS #334 had the good fortune to be assigned to the Palo Alto center, under the direction of Kenneth James, Ph.D. Dr. James, in turn, was responsible for the assignment of the project biostatistician, Ronald Thomas, Ph.D.

Planning and developing a multi-site study involves many different individuals in addition to the Principal Proponent and study biostatistician. Planning committee members are solicited by the Principal Proponent and nominated with the approval of the CSP. Our planning committee for CS #334 included Edward Blanchard, Ph.D., SUNY-Albany, Roger Pitman, M.D., and Scott Orr, Ph.D., of the Manchester VA and Harvard Medical School, and Patrick Boudewyns, Ph.D., of the Augusta VA, in addition to ourselves.

The Principal Proponent for the study assumes leadership in the planning process and is actively involved in the nomination and selection of members of the planning committee. He or she serves as the chair for the planning meetings and has primary responsibility for coordination and writing of the full proposal for submission. Unlike other grants that are submitted to funding agencies exclusively as paper documents, the Cooperative Studies Program offers the Principal Proponent and the study biostatistician the opportunity to defend their proposal orally before the Cooperative Studies Evaluation Committee (CSEC). This oral presentation gives the Principal Proponent a forum in which to emphasize details that may be of special importance and to answer questions that members of the CSEC have regarding the application. The biostatistician is likely to be called upon to defend the choice of study design and data analytic strategies. Without question this is one of the more challenging experiences of heading a Cooperative Study.

The real excitement begins when a Cooperative Study proposal finishes the review process with highly favorable ratings and is designated to receive funding.

Typically, a study is funded to establish and maintain a Study Chair's office, a local entity under the direction of the Principal Proponent that serves to monitor and administrate the conduct of the study itself. Our Study Administrator was Adele George, R.N., an experienced research nurse. One of her initial tasks was to work closely with the Study Chair and the biostatistician to solicit study-site investigators. For CS #334, forty-five applications were submitted by investigators from across the country, with fifteen sites ultimately selected to receive funding to participate. Important considerations in these decisions were the research accomplishments of the potential site investigator, the availability of suitable sources for subject recruitment at a site, and contribution to the geographic mix of the study.

The next phase of the Cooperative Study is to provide education about and training in the research protocol and procedures so that staff at all participating sites are administering the protocol in as near an identical fashion as possible. Our training program consisted of two phases.

First, we convened a three-day meeting in New Orleans to train staff from all sites, particularly the study clinicians, in the details of participant selection and screening. As part of the training, research technicians were taught the use of the psychophysiological equipment in the context of the protocol we had designed. The second phase involved on-site training at which Danny Kaloupek or Scott Orr set up each laboratory and reviewed the study methods with the local study staff. Throughout the study, Adele George provided daily supervision of all 15 study sites, answering questions and resolving problems in a manner that aimed to maintain a high level of procedural consistency and integrity.

The Executive Committee of a Cooperative Study always includes the Principal Proponent and the Study Biostatistician as well as a small group of investigators who are actively involved in the research study either as participating investigators or specialized consultants. The Executive Committee is the overall managing body that makes decisions for operational components of the study. Any changes in protocols are made by the Executive Committee, and this group typically has the final word on publications regarding study data. For CS #334, many of the

members of the Planning Committee also agreed to serve on the Executive Committee.

The Data Monitoring Board (DMB) consists of experts in the subject matter of the project as well as external biostatisticians and other personnel with appropriate scientific skills. A DMB is responsible for monitoring, evaluating, and making recommendations regarding aspects of the ongoing study. In contrast to the Executive Committee, which is blinded with regard to the interim data analyses, DMB members are informed about interim findings as the study progresses. This oversight is particularly important when clinical procedures with life and death implications are involved. It evaluates at periodic intervals whether the study should continue, assesses the performance of each data collection site, makes recommendations regarding their continued participation, and provides recommendations to the Executive Committee regarding changes in the protocol. The Study Chair nominates candidates for the Board, but members are selected by the CSP personnel.

Among the challenging aspects of conducting our Cooperative Study was gaining approval from the 15 Human Studies Committees (HSM) at participating VA Medical Centers, as well as the HSC for the Cooperative Studies Program itself. This latter committee had overarching responsibility for determining that the protocol was safe and consistent with the interests and welfare of participants. However, it was also necessary to work with the local HSC and to address their individual questions and concerns. We were fortunate to have site investigators who already had excellent relationships with their local HSC and were able to resolve this complex set of dictates in a manner that allowed a uniform protocol to be implemented.

The CSP Human Studies Committee met with the Data Monitoring Board annually during the study to follow the course of data collection. While CS #334 did not encounter difficulties in this regard, it is possible for the HSC to recommend changes in the protocol because of problems that emerge during implementation, or to even terminate a study if participants' well-being is compromised.

It should be apparent that completing a successful Cooperative Study is a complex process involving individuals at the study sites, the Coordinating Center, and the Chair's office. In addition, the DMB and the HSC work with the Executive Committee to identify problems that might undermine successful study completion. Difficulties at any site or with the protocol as a whole are managed immediately by one or another of these Committees.

Most Cooperative Studies take several years to complete. As a result, there are often personnel changes at study sites. In the case of CS #334, these changes included site investigators, study clinicians, and study technicians. Our study also had the less typical experience of having personnel changes in the CSP office itself. Along the way, Philip Lavori, Ph.D., became the director of the Palo Alto center and Frank Hsieh, Ph.D., became the study biostatistician. It is a testament to the professionalism of both original and new CSP staff that the study was able to succeed despite these major transitions.

In summary, the VA Cooperative Studies Program offers a unique opportunity to address large-scale questions in a system that shares many common characteristics in terms of patients, staffing, and service delivery. Participating in a Cooperative Study at any level provides the investigator with a perspective on health care and on science that is otherwise difficult to attain. Many of the investigators who were actively involved in the Cooperative Study on the psychophysiology of PTSD stated forthrightly that the experience was among the best scientific efforts with which they had been involved over the course of their careers. Thus, while the process is complex, the rewards of research within the Cooperative Studies framework are many, both for the individuals involved and for the body of scientific knowledge to which they are contributing with their efforts.

Looking ahead, Cooperative Study #420 is a multi-site trial investigating group therapy in PTSD. It is chaired by Matthew Friedman, M.D., Ph.D., and Paula Schnurr, Ph.D., of the National Center for PTSD in White River Junction, VT. These investigators have successfully launched the largest treatment study of PTSD proposed to date and perhaps one of the most important examinations of group therapy in the treatment of any psychological condition. We wish the proponents and the study site investigators the best of luck in completing their clinical trial.

ABOUT THE VA COOPERATIVE STUDIES PROGRAM

Cooperative studies first began in the VA system in 1946, with landmark research in the treatment of tuberculosis. This research established a framework that evolved into the present-day Cooperative Studies Program. The Cooperative Studies Program (CSP) was established as a division of the Medical Research Service in 1972. Traditionally, it has coordinated multi-center clinical trials of new therapies or new uses for standard treatments. In 1990, a program to facilitate multi-site health services research, Cooperative Studies in Health Services, was created within the Health Services Research and Development Service. In 1996, these programs were merged, and the Cooperative Studies Program became the fourth service in the VA's Office of Research and Development. The program's mission now encompasses all fields of research important to veteran's health care: medical research, health services research, and rehabilitation research.

CSP utilizes the power of multi-center studies to achieve more definitive findings than might be available in single-site studies. With its many hospitals and integrated networks, the Veterans Health Administration is an ideal place to conduct large-scale cooperative research. Such work has a direct impact on veterans' clinical care, and provides a national resource to the health-care community within the VA and beyond.

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RESEARCH AT THE NATIONAL CENTER FOR PTSD: CLINICAL LABORATORY AND EDUCATION DIVISION

Kent D. Drescher, PhD

The National Center for PTSD Clinical Laboratory in Menlo Park, California, provides and studies both inpatient and outpatient clinical services. Currently there are men's (48-bed) and women's (10-bed) inpatient programs. These programs provide intensive 45-day multi-modal inpatient care. Group psychotherapy focuses on developing more successful here-and-now coping skills and life plans, and typically includes group trauma focus. In the outpatient setting, the PTSD Clinical Team (PCT) staff provide outpatient assessment and treatment at four locations: Menlo Park, San Jose, Santa Cruz, and Monterey.

Dr. Kent Drescher is currently collecting data for an inpatient program evaluation protocol. Previous research by Ford (1995) found clinician ratings of patient object-relations to predict treatment outcome. The present study is an attempt to replicate and extend this finding. PTSD and associated symptom severity, social support, coping, and quality of life are being monitored. All patients are assessed at admission, discharge, and follow-up. Approximately 40 patients have completed the protocol. Dr. Ron Murphy is collecting pilot data on the effectiveness of a group treatment designed to increase awareness of and motivation to change PTSD-related problem behaviors. Early data indicates that many patients do not perceive a need to change various PTSD symptoms, especially anger and isolation. Non-confrontational motivational interviewing techniques appear useful in enhancing patient awareness of the need to change various problem behaviors. It is hoped that post-treatment outcome for PTSD patients may improve with increased patient willingness to change problem behaviors. Dr. Murphy is also completing a manuscript describing findings from an NIAAA-funded study of the effects of combat exposure and childhood trauma on alcohol use. Results suggest that a history of severe physical punishment as a child correlates with higher combat exposure. Also, compared to childhood trauma, combat exposure is a better predictor of past-year alcohol consumption. Finally, IRB approval has been received for analysis of findings related to clinical assessment data collected on patients who received inpatient treatment between 1990 and 1996. Dr. Drescher and other NCPTSD staff plan a series of articles to describe these data. Database and staffing infrastructure have been developed to begin efficiently evaluating outcomes for outpatients treated by our PCT program at all four sites. We hope to submit a protocol shortly to begin monitoring outcomes in this setting.

Dr. Steve Woodward directs the NCPTSD Sleep Laboratory. This lab is in year two of a three-year Merit Review Grant designed to record PTSD nightmares and to assess the physiologic background of waking intrusive phenomena such as intrusive thoughts and flashbacks. In this context he has initiated 24-hour ambulatory monitoring in PTSD inpatients. This project will also provide precise estimates of the contribution of physical activity to 24-hour integrated urinary norepinephrine, epinephrine, and cortisol. This laboratory is engaged in the development of two advanced diagnostic methodologies for application to PTSD. The first is an enhanced trauma cue reactivity protocol which assesses patients' arousal responses to visual and auditory reminders of their traumatic experiences. The second is an auditory version of the emotional Stroop paradigm, which assesses the degree to which trauma-related cues deflect a patient's attentional resources from a primary task. Additionally, the lab is involved in a formal collaboration with Richard J. Ross's NIH-funded examination of sleep in monozygotic twins discordant for PTSD.

Dr. Annabel Prins is involved in the development and validation of a 4-item PTSD screening instrument for use in primary-care settings. Currently data are being collected in two primary-care clinics. The protocol involves administration of the PTSD screen followed by a CAPS interview. Preliminary data indicate that a high percentage of veterans in primary-care clinics have trauma exposure. The screen instrument appears to have good internal consistency, adequate test-retest reliability, and adequate concurrent validity with the CAPS interview. To date, 29% of veterans screened meet criteria for full PTSD, and 48% have partial PTSD symptoms. In addition, Dr. Prins's other research projects include survey research on the reasons and consequences of trauma concealment, laboratory research on possible moderators of psychophysiological responding in PTSD, and archival research on lipid levels in women with and without PTSD.

Selected Bibliography

ABUEG, F.R., DRESCHER, K.D., & KUBANY, E.S. (1994). **Natural disasters.** In F.M. Dattilio & A. M. Freeman (Eds.), *Cognitive-behavioral strategies in crisis intervention* (pp. 238-257). NY: Guilford Press.

GUSMAN, F.D., STEWART, J., YOUNG, B.H., RINEY, S.J., ABUEG, F.R., & BLAKE, D.D. (1996). **A multicultural developmental approach for treating trauma.** In A.J. Marsella, M.J. Friedman, E.T. Gerrity, & R.M. Scurfield (Eds.), *Ethnocultural aspects of posttraumatic stress disorder: Issues, research, and clinical applications* (pp. 439-457). Washington, DC: American Psychological Association.

SEIDEL, R.W., GUSMAN, F.D., & ABUEG, F.R. (1994). **Theoretical and practical foundations of an inpatient post-traumatic stress disorder and alcoholism treatment program.** *Psychotherapy, 31,* 67-78.

WOODWARD, S.H., DRESCHER, K.D., MURPHY, R.T., RUZEK, J.I., FOY, D.W., & ARSENAULT, N.J. (1997). **Heart rate during group flooding therapy for PTSD.** *Integrative Physiological and Behavioral Science, 32,* 19-30, 75-83.

WOODWARD, S.H., WANG, S., MASON, J.W., & ARSENAULT, N.J. (1997). **Prediction of REM sleep percent in PTSD.** *Sleep Research, 26,* 306.

ZAIDI, L.Y. & FOY, D.W. (1994). **Childhood abuse experiences and combat-related PTSD.** *Journal of Traumatic Stress, 7,* 33-42.

PILOTS UPDATE

With the next update to the PILOTS database, scheduled for the end of April, we shall be using many new descriptors to indicate more precisely the subject-matter of the publications we are indexing. These new descriptors, as well as changes to existing ones, will be included in a revision of the PILOTS Thesaurus. A preliminary version of this will appear on our Web site at the beginning of May. Later this year a new version of the *PILOTS Database User's Guide* will be published in print and on the Web.

Changing a controlled indexing vocabulary is a difficult process, requiring careful examination of the existing literature, educated guesses as to its future development, and time-consuming consultation with experts in specialized areas.

If it is decided to apply changes retrospectively, the burden increases. It is necessary to conduct many searches of the existing database, examine the documents retrieved by these searches, decide in which cases existing indexing must be modified, and then enter the changes in the affected records. This is so laborious a process that many databases do not apply changes to their indexing vocabularies to existing records. Users of the PsycINFO database have to consult the *Thesaurus of Psychological Indexing Terms* to learn, for example, that they must "use TRAUMATIC NEUROSIS or STRESS REACTIONS to access references from 1973-1984" because the descriptor POSTTRAUMATIC STRESS DISORDER was not added to the Thesaurus until 1985.

Other databases, most notably MEDLINE, revise their indexing vocabularies frequently and then apply these changes to all records. Each year when the new edition of *Medical Subject Headings* is published, changes are made throughout the database to reflect the new MeSH terms. In order to make searching the traumatic stress literature as easy as possible for our users, we are following this model in the PILOTS database.

What sort of changes are we making in our indexing vocabulary?

Many of the new terms will make it easier to find publications on specific populations affected by traumatic events. These include ethnic groups such as AMERASIANS, HMONG, and MIEN; occupational groups such as AGRICULTURAL WORKERS, JOURNALISTS, and RELIEF WORKERS; religious groups such as BUDDHISTS, MUSLIMS, ROMAN CATHOLICS, and SIKHS; and other categories such as GRANDCHILDREN, RUNAWAYS, and RURAL POPULATIONS.

We are adding several new descriptors for traumatic events, including DENTAL PROCEDURES, GENITAL MUTILATION, JURY SERVICE, STALKING, and WORKPLACE VIOLENCE. To enhance retrieval of publications on the effects of exposure to such events, we are adding ATTACHMENT BEHAVIOR, GASTROINTESTINAL SYMPTOMS, MULTIPLE CHEMICAL SENSITIVITY, and SHAME. And we shall be using the descriptors TRAUMATIC NEUROSES and WAR NEUROSES to describe the content of literature from before the DSM era. In the areas of assessment and treatment, we are adding CROSS CULTURAL ASSESSMENT, DRAMA THERAPY, MANUAL-BASED TREATMENTS, THOUGHT FIELD THERAPY, TWELVE STEP PROGRAMS, and others.

We are also changing some existing descriptors to make them more useful in searching. Publications previously indexed under PSYCHOANALYSIS will instead be assigned PSYCHOANALYTIC THEORY or PSYCHOANALYTIC PSYCHOTHERAPY. We shall use the new descriptor DISSOCIATIVE SYMPTOMS to describe studies reporting sequelae of traumatic events that do not meet DSM criteria for the full-blown disorder, leaving the existing descriptor DISSOCIATIVE DISORDERS to be used in a more narrow sense.

These are only a few of the changes that we shall be making in our indexing vocabulary, and it is possible that some of these will appear in different form in the new PILOTS Thesaurus. Our hope—and our reason for undertaking this laborious effort—is that these changes will make it easier to use the PILOTS database to find the information needed by researchers, clinicians, and others concerned with PTSD and other disorders associated with exposure to traumatic events.

Please remember that these changes will take effect only with the April update to the database. Until the end of April, continue to use the existing PILOTS Thesaurus as contained in the *Pilots Database User's Guide,* Second Edition, November 1994.

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